

**PATENT**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:

David P. Bingaman  
Abbot F. Clark  
Rajni Jani  
Stella M. Robertson

Serial No.: 10/772,963 (Conf. #5299)

Filed: February 3, 2004

For: FORMULATIONS OF  
GLUCOCORTICOIDS TO TREAT  
PATHOLOGIC OCULAR  
ANGIOGENESIS

Group Art Unit: 1617

Examiner: S. Hui

Atty. Dkt. No.: 2471 US

**APPEAL BRIEF**

Mail Stop Appeal Brief-Patents  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

This paper is submitted in response to the Final Office Action dated February 14, 2006, for which the three-month date for response was May 14, 2006. A Response to the Final Office Action was timely filed on May 15, 2006. Appellants did not receive an Advisory Action. A Notice of Appeal was timely filed by First Class mail on August 14, 2006. The due date for this Appeal Brief was October 18, 2006, by virtue of the Notice of Appeal being received in the USPTO on August 18, 2006, as evidenced in the return postcard (a copy of which is included herewith as Exhibit A).

A request for a three-month extension of time to file the Appeal Brief is included herewith along with the required fee. This three-month extension will bring the due date to

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January 18, 2007, which is within the six-month statutory period. Should such request for extension or fee be deficient or absent, consider this paragraph such a request and authorization to withdraw the appropriate fee under 37 C.F.R. §§ 1.16 to 1.21 from Alcon, Inc. Deposit Account No. 501051.

**I. REAL PARTY IN INTEREST**

The real party in interest in this case is Alcon, Inc.. The recordation of assignment documents are attached hereto as Exhibit B.

**II. RELATED APPEALS AND INTERFERENCES**

Appellants know of no related appeals or interferences.

**III. STATUS OF CLAIMS**

Claims 1-2 were originally filed with the case. Claims 3-18 were added in a Response to Office Action filed on March 9, 2005. Claims 1, 3, 4, 6, 8, 10, and 16 were amended and claim 2 was canceled in a Response to Office Action dated November 15, 2005. A Final Office Action rejecting all claims was mailed on February 14, 2006. No claims were amended, added, or canceled in the Response to Final Office Action filed May 15, 2006. The Appellants did not receive an Advisory Action.

Thus, claims 1 and 3-18 are the subject of this Appeal. The Appealed claims are set forth in the Claims Appendix.

**IV. STATUS OF AMENDMENTS**

No claims were amended, added or canceled in the Response to Final Office Action filed on May 15, 2006. There are no outstanding amendments to the claims.

**V. SUMMARY OF CLAIMED SUBJECT MATTER**

The present invention is directed to methods for treating pathologic ocular angiogenesis using certain formulations of glucocorticoids in combination with anecortave acetate (Spec. page 2, lines 34-36). Preferred glucocorticoids for use in the methods of the present invention include triamcinolone acetonide, prednisolone, prednisolone acetate, rimexolone, fluoromethalone, and fluoromethalone acetate (Spec. page 4, lines 10-34). Where triamcinolone acetonide is the glucocorticoid employed in the formulation used in the methods of the invention, the preferred concentration of triamcinolone acetonide in the composition is from 0.4% to 2.0% w/v (Example 1). Where rimexolone is the glucocorticoid employed in the formulation used in the methods of the invention, the preferred concentration of rimexolone in the composition is from 0.1% to 4.0% w/v (Example 2). Where prednisolone acetate is the glucocorticoid employed in the formulation used in the methods of the invention, the preferred concentration of prednisolone acetate is from 0.1% to 2.0% w/v (Example 3). Where fluoromethalone acetate is the glucocorticoid employed in the formulation used in the methods of the invention, the preferred concentration of fluoromethalone acetate is from 0.1% to 1.0% w/v (Example 4). The preferred concentration of anecortave acetate in the compositions used in the methods of the invention is from 0.1% to 6.0% w/v. More preferably, the concentration of anecortave acetate in the compositions of the invention is from 1% to 3% w/v. Most preferably, the concentration of anecortave acetate in the compositions of the invention is 3% w/v. (Examples 5 and 6).

For the treatment of pathologic ocular angiogenesis, the compositions of the invention are preferably administered via intravitreal injection, posterior juxtascleral delivery,

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subconjunctival injection, or an implanted device (Spec. page 4, lines 36-38). The compositions are preferably administered via posterior juxtascleral delivery (Spec. page 6, lines 24-28) or via an implaned device (Spec. page 5, line 1 to page 6, line 22).

## **VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL**

- 1. Whether claims 1-5 and 8-18 are obvious over the combination of Peyman (U.S. Patent No. 5,516,522) and Clark (U.S. Patent No. 5,770,592).**
- 2. Whether claims 1-2, 4-5 and 16-18 are obvious over the combination of WO95/03807 ('807) and Clark (U.S. Patent No. 5,770,592).**
- 3. Whether claims 1-3, and 6-7 are obvious over the combination of Clark (U.S. Patent No. 5,770,592) and Boltralik (U.S. Patent No. 4,686,214).**

## **VII. ARGUMENT**

### **A. The Claims are Patentable Over Peyman and Clark**

The Final Action rejects claims 1-5 and 8-18 as being obvious over U.S. Patent No. 5,516,522 (Peyman) and Clark. Peyman is said to teach prednisolone, prednisolone acetate, triamcinolone, fluoromethalone, and fluoromethalone acetate as useful in treating proliferative vitreoretinopathy and that the ocular formulation may be an intraocular implant. Clark is said to teach anecortave acetate as useful in treating ocular neovascularization. The Final Action acknowledges that the references taken together do not expressly teach the incorporation of both steroids and anecortave acetate together in a method of treating angiogenesis disorders, nor do they teach the claimed dosages. Nevertheless, the Final Action

asserts that it would have been obvious to combine the references because each element was known separately. Appellants respectfully traverse.

As pointed out in the Response filed November 15, 2005, Peyman appears to describe a biodegradable drug delivery device designed to solve the problem of prolonged drug release into the vitreous of the eye that does not have to be removed after all of the drug in the device has been delivered to the desired site. While Peyman mentions the potential use of steroids in the device described therein, it does not provide any teaching or suggestion of dosage amounts of particular steroids for the treatment of pathologic ocular angiogenesis. Nor does Peyman contain any mention of the use of anecortave acetate with the steroids for the treatment of pathologic ocular angiogenesis.

The issue is whether the subject matter claimed would have been obvious, at the time of the present invention, to one of ordinary skill in the art. The question is not whether using two different compounds to treat pathologic ocular angiogenesis is obvious, but rather, whether using two different compounds in the same composition is obvious. It is clear that the proper approach to the obviousness issue must start with the claimed invention as a whole. 35 U.S.C. § 103; *Gillette Co. v. S.C. Johnson & Son, Inc.*, 919 F.2d 720, 724 (Fed. Cir. 1990). While it may be true that the present invention consists of a combination of old elements so arranged as to perform certain related functions, that is immaterial to the issue. It is well settled that “what must be found obvious to defeat the patent is the claimed combination.” *Id.* (quoting *Kimberly-Clark Corp. v. Johnson & Johnson*, 745 F.2d 1437, 1448, 223 U.S.P.Q. 603, 609-10 (Fed. Cir. 1984) (emphasis added)).

At best, Peyman suggests that two different active agents could be delivered through the described device in essentially separate compositions. Peyman states that “one agent incorporated at one end of the porous device may be allowed to be released quickly by fabricating one end of the porous device with a high channel density. The other end of the porous device could have a lower channel density and the pharmacological agent at that end would be released slowly.” (col. 8, lines 28-33). Clearly, Peyman’s device was intended for use with a single active agent, which could be delivered over a prolonged period of time through a device that will completely degrade within the body so that further surgery to remove the device is not required. The language cited above amounts to nothing more than a suggestion to try to add a second active agent, providing no expectation of success, especially if the second agent is contained within the same composition as the first active agent.

Appellants point out that “obvious to try” is not the proper standard for a *prima facie* finding of obviousness. “An ‘obvious-to-try’ situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued. *Gillette*, 919 F.2d at 725 (citing *In re Eli Lilly & Co.*, 902 F.2d 943, 945, 14 USPQ2d 1741, 1743 (Fed.Cir.1990)). The *Gillette* court explained that an understanding of the particular results achieved is critical to the analysis of obviousness. *Id.* The present invention is directed to a method of treating pathologic ocular angiogenesis by administering a single composition comprising a glucocorticoid and anecortave acetate. Glucocorticoids are known to produce significant side effects, including endophthalmitis, cataracts, and elevated

intraocular pressure, when used alone. The formulations of the present invention are intended to provide effective treatment of pathologic ocular angiogenesis while causing no or lessened adverse reactions. It would not have been obvious to the skilled artisan that administering a glucocorticoid with a second anti-angiogenic agent would solve the problem of the unwanted side effects. Nothing within Peyman suggests that adding anecortave acetate to the composition containing the glucocorticoid would solve the problem of unwanted side effects.

The Final Action has failed to provide evidence of motivation to the skilled artisan to combine the teachings of the cited references to arrive at a method of treating pathologic ocular angiogenesis by administering a single composition containing a glucocorticoid and anecortave acetate. Rather, the Final Action has simply restated the position that it would have been obvious because the two compounds have been used separately. The Federal Circuit has clearly established that this is not the proper inquiry for obviousness (*see Gillette and Kimberly Clark supra*).

In light of the foregoing arguments, Appellants respectfully request that the obviousness rejection based upon Peyman and Clark be withdrawn.

**B. The Claims are Patentable Over WO95/03807 and Clark**

The Final Action next rejects claims 1-2, 4-5 and 16-18 as being unpatentable over WO 95/03807 ('807) and Clark. Reference '807 is said to teach a method of treating neovascular macular degeneration by administration of triamcinolone and that the drug may be administered by intravitreal injection. Clark is said to teach a method of treating ocular neovascularization disorders using anecortave acetate. The Final Action acknowledges that the references taken together do not teach the incorporation of both the triamcinolone and anecortave acetate together in a method of treating angiogenesis disorders. The Final Action asserts that it would have been

obvious to incorporate triamcinolone and anecortave acetate together in a method of treating angiogenesis disorder. Appellants respectfully traverse.

As with the rejection discussed above, the rejection of the claims as being obvious over the '807 reference and Clark amounts to a statement that it would have been obvious to combine the two compounds for the treatment of pathologic ocular angiogenesis because each compound was known separately. At best, the Action's position is that it would have been obvious to try to make and use the claimed combination of compounds. Appellants arguments provided above with respect to the obviousness rejection based upon Peyman and Clark apply equally with respect to the rejection based on the '807 reference and Clark. Neither reference mentions the claimed combination for the treatment of pathologic ocular angiogenesis, as the Final Action admits. According to the established caselaw, a clear explanation of the motivation for the combination is required in order to establish obviousness. That explanation has not been provided.

In light of the foregoing arguments, Appellants respectfully request that the obviousness rejection based on the '807 reference and Clark be withdrawn.

**C. The Claims are Patentable over Clark and Boltralik**

Claims 1-3 and 6-7 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Clark and Boltralik. Clark is said to teach anecortave acetate as useful in treating ocular neovascularization inflammatory conditions and to teach that the composition can be formulated and administered as an intraocular injection. Boltralik is said to teach rimexolone as useful in treating ocular inflammation with an effective dosage of 0.05 to 2.0%. The Final Action acknowledges that the references taken together do not expressly teach the

incorporation of both rimexolone and anecortave acetate together in a method of treating angiogenesis inflammatory disorders, nor do they expressly teach the claimed dosages. Nevertheless, the Final Action reasons that it would have been obvious to one of ordinary skill in the art to incorporate both rimexolone and anecortave acetate together in a method of treating angiogenesis inflammatory disorder and to employ the claimed dosages. The Final Action argues that the motivation to combine rimexolone and anecortave acetate for the treatment of angiogenesis inflammatory disorders comes from the agents each being known for treating inflammation individually. Appellants respectfully traverse.

It appears that Boltralik seeks to solve the problem of ophthalmic inflammatory disorders by administering a certain steroid that is known not to adversely affect IOP. Boltralik does not suggest combining such steroids with a second agent, much less with anecortave acetate. In fact, the present invention seeks to solve the problem of adverse side effects, including elevated IOP, associated with the use of steroids. Since Boltralik asserts that the steroids described therein for use in treating ophthalmic inflammation lack IOP elevating effects, Boltralik effectively teaches away from combining those same steroids with an additional agent that will control any IOP rise associated with the use of the glucocorticoid.

The Final Action has failed to provide evidence of motivation to the skilled artisan to combine the teachings of the cited references to arrive at a method of treating pathologic ocular angiogenesis by administering a single composition containing a glucocorticoid and anecortave acetate.

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In light of the foregoing arguments, Appellants respectfully request that the obviousness rejection based on Clark and Boltralik be withdrawn.

**D. Conclusion**

This is submitted to be a complete Brief on Appeal.

The Examiner is invited to contact the undersigned attorney at (817) 551-4321 with any questions, comments or suggestions relating to the referenced patent application.

### **VIII. CLAIMS APPENDIX**

The claims on appeal are as follows:

1. A method for treating pathologic ocular angiogenesis and any associated edema which comprises, administering a composition comprising an effective amount of a glucocorticoid and an effective amount of anecortave acetate.
2. (canceled)
3. The method of claim 1, wherein the glucocorticoid is selected from the group consisting of triamcinolone acetonide, prednisolone, prednisolone acetate, rimexolone, fluoromethalone, and fluoromethalone acetate.
4. The method of claim 3, wherein the glucocorticoid is triamcinolone acetonide.
5. The method of claim 4, wherein the concentration of triamcinolone in the composition is from 0.4% to 2.0% w/v.
6. The method of claim 3, wherein the glucocorticoid is rimexolone.
7. The method of claim 6, wherein the concentration of rimexolone in the composition is from 0.1% to 4.0% w/v.
8. The method of claim 3, wherein the glucocorticoid is prednisolone acetate.
9. The method of claim 8, wherein the concentration of prednisolone acetate in the composition is from 0.1% to 2.0% w/v.
10. The method of claim 3, wherein the glucocorticoid is fluoromethalone acetate.

11. The method of claim 10, wherein the concentration of fluoromethalone acetate in the composition is from 0.1% to 1.0% w/v.

12. The method of claim 3, wherein the composition comprises anecortave acetate and triamcinolone acetonide.

13. The method of claim 12, wherein the concentration of anecortave acetate in the composition is from 0.1% to 6% w/v and the concentration of triamcinolone acetonide in the composition is from 0.5% to 4.0% w/v.

14. The method of claim 13, wherein the concentration of anecortave acetate in the composition is from 1% to 3% w/v.

15. The method of claim 14, wherein the concentration of anecortave acetate in the composition is 3% w/v.

16. The method of claim 1, wherein the composition is delivered by intravitreal injection, posterior juxtascleral delivery, subconjunctival injection, or via an implanted device.

17. The method of claim 16, wherein the composition is delivered by posterior juxtascleral injection.

18. The method of claim 16, wherein the composition is delivered via an implanted device.

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**IX. EVIDENCE APPENDIX**

None

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**X. RELATED PROCEEDINGS APPENDIX**

None

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Respectfully submitted,

/Teresa J. Schultz, Reg. #40,526/

Teresa J. Schultz  
Reg. No. 40,526  
Attorney for Applicants

ALCON RESEARCH, LTD.  
6201 S. Freeway, Q-148  
Fort Worth, TX 76134-2099  
(817) 551-4321

Date: January 18, 2007

**EXHIBIT A**

**THE OFFICIAL DATE STAMP HEREON BY THE USPTO  
ACKNOWLEDGES RECEIPT OF THE FOLLOWING:**

**Title:** Formulations Of Glucocorticoids To Treat Pathologic Ocular Angiogenesis

**Applicant:** David P. BINGAMAN

**Application No.:** 10/772,963 (Corr #5299)

**Date of Filing Paper:** 14 August 2006

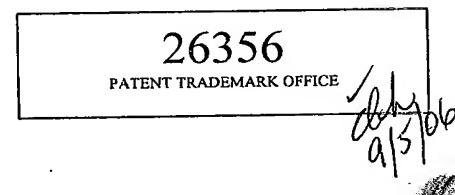
**Enclosures:**

- (1) Transmittal [1 pg];
- (2) Notice Of Appeal [1 pg, in duplicate];
- (3) Petition for Extension Of Time [1 pg, in duplicate]; and
- (4) Return Card.

**Docket No.:** 2471 US

**Initials:** TJS/bmc

**First Class Mail**



**EXHIBIT B**



**UNITED STATES PATENT AND TRADEMARK OFFICE**

**UNDER SECRETARY OF COMMERCE FOR INTELLECTUAL PROPERTY AND  
DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE**

AUGUST 10, 2004

PTAS



\*102668434A\*

ALCON RESEARCH, LTD.  
TERESA J. SCHULTZ  
R&D LEGAL COUNSEL, Q-148  
6201 SOUTH FREEWAY  
FORT WORTH, TX 76134-2099

UNITED STATES PATENT AND TRADEMARK OFFICE  
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

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RECORDATION DATE: 02/05/2004

REEL/FRAME: 014966/0454  
NUMBER OF PAGES: 6

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR: BINGAMAN, DAVID P. DOC DATE: 01/30/2004

ASSIGNOR: CLARK, ABBOT F. DOC DATE: 01/30/2004

ASSIGNOR: JANI, RAJNI DOC DATE: 01/30/2004

ASSIGNOR: ROBERTSON, STELLA M. DOC DATE: 01/30/2004

ASSIGNEE:  
ALCON, INC.  
P.O. BOX 62, BOSCH 69  
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AUG 16 2004

014966/0454 PAGE 2

SERIAL NUMBER: 10772963

FILING DATE: 02/05/2004

PATENT NUMBER:

ISSUE DATE:

TITLE: FORMULATIONS OF GLUCOCORTICOIDS TO TREAT PATHOLOGIC OCULAR  
ANGIOGENESIS

THERESA FREDERICK, EXAMINER  
ASSIGNMENT DIVISION  
OFFICE OF PUBLIC RECORDS

02-13-2004

Form PTO-1595  
(Rev. 10/02)

OMB No. 0651-0027 (exp. 6/30/2005)

2504

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To the Honorable Commissioner of Patents and Trademarks: Please record the attached original documents or copy thereof.

  
10/772963  
020504

1. Name of conveying party(ies):  David P. Bingaman, Abbot F. Clark, Rajni Jani and Stella M. Robertson	2. Name and address of receiving party(ies)  Name: Alcon, Inc.  Internal Address:  Street Address:  P.O. Box 62, Bösch 69  City: Hünenberg State: Switzerland Zip: CH-6331
Additional name(s) of conveying party(ies) attached? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
3. Nature of conveyance:  <input checked="" type="checkbox"/> Assignment <input type="checkbox"/> Merger <input type="checkbox"/> Security Agreement <input type="checkbox"/> Change of Name <input type="checkbox"/> Other _____	
Execution Date: 01/30/2004	Additional name(s) & address(es) attached? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

4. Application number(s) or patent number(s):  
 If this document is being filed together with a new application, the execution date of the application is: 02/05/2004

A. Patent Application No.(s)

10772963

B. Patent No.(s)

Additional numbers attached?  Yes  No

5. Name and address of party to whom correspondence concerning document should be mailed:  Name: Teresa J. Schultz  Internal Address:  Alcon Research, Ltd.  R&D Legal Counsel, Q-148  Street Address:  6201 South Freeway  City: Fort Worth State: TX Zip: 76134-2099	6. Total number of applications and patents involved: 1  7. Total fee (37 CFR 3.41).....\$ 40.  <input type="checkbox"/> Enclosed <input checked="" type="checkbox"/> Authorized to be charged to deposit account
8. Deposit account number:  501051	(Attach duplicate copy of this page if paying by deposit account)

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## 9. Statement and signature.

*To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.*

Teresa J. Schultz, Reg. No. 40,526

Name of Person Signing

  
Signature


  
Date

Total number of pages including cover sheet, attachments, and documents: 6

Mail documents to be recorded with required cover sheet Information to:  
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 Washington, D.C. 20231

Docket #2471 US

2/13/2004 LMUELLER 00000036 501051 10772963

I FC:8021 40.00 DA

**A S S I G N M E N T**

WHEREAS I am a below named joint inventor of the invention entitled:

FORMULATIONS OF GLUCOCORTICOIDS TO TREAT  
PATHOLOGIC OCULAR ANGIOGENESIS

and described in a United States Patent Application filed with the United States Patent and Trademark Office on February 5, 2004, and further identified by Attorney Docket No. 2471 US; and

WHEREAS, ALCON, INC., having a place of business at P. O. Box 62, Bösch 69, CH-6331 Hünenberg, Switzerland, is desirous of acquiring the entire right, title and interest in and to said invention and to any and all Letters Patent of the United States and foreign countries which may be obtained therefor;

NOW, THEREFORE, for good and valuable consideration, I do hereby sell, assign and transfer to ALCON INC., its legal representatives, successors, and assigns, the entire right, title and interest in and to said invention as set forth in the above-mentioned application, and in and to any and all patents of the United States and foreign countries which may be issued for said invention;

UPON SAID CONSIDERATIONS, I hereby agree that I will not execute any writing or do any act whatsoever conflicting with these presents, and that I will, at any time upon request, without further or additional consideration but at the expense of said assignee, execute such additional assignments and other writings and do such additional acts as said assignee may deem necessary or desirable to perfect the assignee's enjoyment of this grant and render all necessary assistance in making application for and obtaining original, divisional, continuation-in-part, reexamined, reissued, or other Letters Patent of the United States or of any and all foreign countries on said invention and in enforcing any rights in action accruing as a result of such applications or patents, said assistance to include my cooperation in all prosecution associated with obtaining such applications or patents and my provision of testimony in any proceedings or transactions involving such applications or patents, it being understood that the

foregoing covenant and agreement shall bind, and insure to the benefit of, the assigns and legal representatives of assignor and assignee.

AND I request the Commissioner of Patents and Trademarks to issue any Letters Patent of the United States which may be issued for said invention to said ALCON INC., its legal representatives, successors or assigns, as the sole owner of the entire right, title and interest in said patent and the invention covered thereby.

Full name of joint inventor: David P. BINGAMAN

Address: 901 Meadow Hill Road  
Fort Worth, TX 76018

Inventor's signature:

David P. Big

1/30/04

Date:

Citizenship:

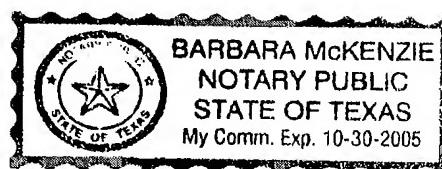
United States of America

STATE OF TEXAS §

COUNTY OF TARRANT §

On this 30th day of January, 2004, before me personally appeared **David P. Bingaman**, to me known to be the person named in and who executed the above instrument, and acknowledged to me he/she executed the same for the uses and purposes therein set forth.

Barbara McKenzie  
Notary Public



Full name of joint inventor:

Abbot F. CLARK

Address:

5603 Rachel Court  
Arlington, TX 76017

Inventor's signature:



Date:

30 January 2004

Citizenship:

United States of America

STATE OF TEXAS

§

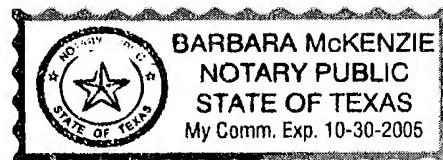
COUNTY OF TARRANT

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§

On this 30th day of January, 2004, before me personally appeared **Abbot F. Clark**, to me known to be the person named in and who executed the above instrument, and acknowledged to me he/she executed the same for the uses and purposes therein set forth.



Barbara McKenzie  
Notary Public



Full name of joint inventor:

Rajni JANI

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Fort Worth, TX 76109

Inventor's signature:

Rajni Jani

Date:

1/30/2004

Citizenship:

United States of America

STATE OF TEXAS §

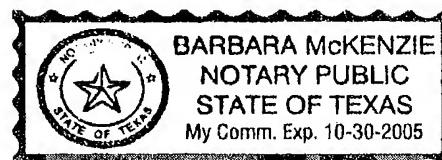
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COUNTY OF TARRANT §

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On this 30th day of January, 2004, before me personally appeared **Rajni Jani**, to me known to be the person named in and who executed the above instrument, and acknowledged to me he/she executed the same for the uses and purposes therein set forth.

Barbara McKenzie  
Notary Public



Full name of joint inventor:

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Address:

7045 Shadow Creek Court  
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Inventor's signature:

Stella M. Robertson  
1/30/2004

Date:

Citizenship:

United States of America

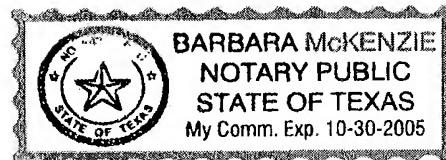
STATE OF TEXAS

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Barbara McKenzie  
Notary Public



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